(19) Europäisches Patentamt
European Patent Office
Office européen des brevets

(11) Publication number: **0 368 408 A2**

(12) EUROPEAN PATENT APPLICATION

(21) Application number: **89202797.0**

(51) Int. Cl.5: **A61F 13/02, A61M 35/00**

(22) Date of filing: **07.11.89**

(30) Priority: **10.11.88 US 269513**

(43) Date of publication of application:
16.05.90 Bulletin 90/20

(84) Designated Contracting States:
AT BE CH DE ES FR GB GR IT LI LU NL SE

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(54) Storage-stable transdermal patch.

(57) A shelf-stable device for transdermally administering an active pharmaceutical to a patient. The device includes a drug reservoir that contains the drug formulation. In one preferred embodiment of the present invention, the drug reservoir is sandwiched between an upper and a lower solvent barrier film that are made from a material such as a polyester that will not absorb the drug and/or skin permeating enhancing solvent, if any, contained within the reservoir. The drug reservoir and solvent barrier films are encapsulated within a hermetically-sealed compartment that protects the drug formulation from common environmental factors such as water vapor, oxygen, and light which can adversely affect the stability and efficacy of the drug formulation. The hermetically-sealed compartment also prevents the drug formulation from coming into contact with and possibly dissolving the adhesive used to secure the device to the patient's skin. In another particularly preferred embodiment of the present invention, the device's drug reservoir is encapsulated within a hermetically-sealed compartment that is made from solvent/environment barrier films that serve the dual functions of preventing the device's components from absorbing the drug/solvent formulation from the reservoir, and protecting the drug/solvent formulation from common environmental factors.

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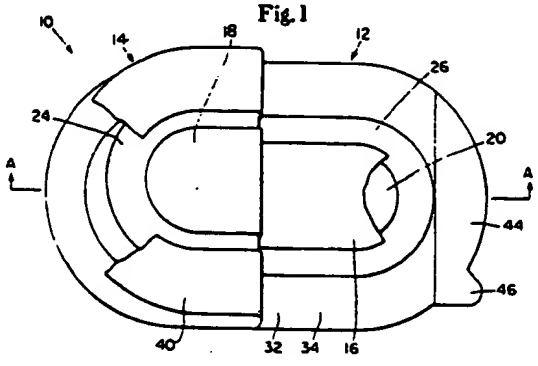
Fig. 1



pending on the drug/skin permeation enhancer formulation, the loss of the lipophilic solvent can significantly decrease the drug's solubility in the formulation and thereby cause the drug to precipitate out while the patch is in storage or during use. In addition, the solvent's loss can significantly reduce the drug flux or absorption rate through the patient's skin. Finally, the solvent entering the packaging material can significantly alter the material's physical properties which can catastrophically impact the integrity of the overall patch structure.

Additional research has shown that common environmental factors such as the presence of moisture, oxygen, and light can adversely affect the stability and efficacy of some drugs and skin permeation enhancers, which in turn can significantly impact the storage stability or shelf life of the transdermal device. For example, it has been found that the solubility of buprenorphine and the lipophilic solvents in some skin permeation enhancers such as propylene glycol decreases significantly if the formulation absorbs even a very small fraction of water. It is also been found that some drugs such as buprenorphine can degrade when exposed to light. Most prior drug delivery device architectures do not specifically address the objective of protecting the drug formulation from common environmental factors.

Most prior transdermal drug delivery devices use a dermatologically-acceptable, pressure-sensitive adhesive to secure the device to a patient's skin. In many of these structures, the drug formulation is allowed to freely come into contact with the adhesive examples of which include U.S. Patent Nos. 3,742,951 to Zaffaroni; 4,144,317 to Higuchi et al.; 4,262,003 to Urquhart et al.; 4,690,683 to Chien et al.; and 4,764,379 to Sanders et al. However, it has been found that many of these adhesives might absorb some skin permeation enhancing agents such as propylene glycol. In addition, it has been found that lipophilic solvents such as methyl laurate and methyl caprylate will swell and even dissolve many adhesives, particularly silicones, polyisobutylenes, and acrylic-based adhesives. Accordingly, many prior transdermal devices are not suitable for containing some types of drug/skin permeation enhancer formulations.

In light of the above, the principal object of the present invention is to provide a transdermal drug delivery system that will uniformly administer a pharmaceutical to a patient in need of such treatment.

Another principal object of the present invention is to construct a transdermal drug delivery device that includes various barrier materials that will not significantly absorb the pharmaceutical and/or a skin permeation enhancer contained therewithin thereby significantly increasing the device's stability and shelf-life.

A further object of the present invention is to construct a transdermal drug delivery device that is made from barrier materials that will significantly increase the shelf life of the device by protecting the drug and/or skin permeation enhancer from common environmental factors such as moisture, oxygen, and light.

Another object of the present invention is to construct a transdermal drug delivery device such that the drug formulation is not exposed to the adhesive used to maintain the device on a patient's skin.

SUMMARY OF THE INVENTION

Transdermal drug delivery devices of the present invention are particularly useful for containing drugs and/or solvents that are not compatible with common packaging materials such as polyolefins or commonly-used pressure-sensitive adhesives. In addition, transdermal devices of the present invention are particularly useful for containing drugs and/or solvents whose stability and efficacy over an extended period of time can be negatively affected if the drug formulation is exposed to common environmental factors such as moisture, oxygen, and light.

In one preferred embodiment of the present invention, the transdermal drug delivery device includes a lower subassembly that holds a drug reservoir, and an upper subassembly. The drug reservoir, which contains the drug formulation, is sandwiched between an upper solvent barrier film and a lower solvent barrier film. These solvent barrier films are preferably made from a material such as a polyester that will not absorb the drug formulation and volatile solvents contained within the reservoir to a significant degree.

The drug reservoir and upper and lower solvent barrier films are hermetically sealed within a protective compartment having a top cover and a bottom cover. The compartment's bottom cover is attached to an adhesive-coated coverstock while the compartment's top cover is attached to a release liner. The bottom surface of the release liner is in contact with the coverstock's adhesive layer that extends beyond the compartment's bottom cover.

In use, the user peels the device's upper subassembly away from the lower subassembly, which breaks the compartment hermetic seal and exposes the drug reservoir. The lower subassembly is then applied to the patient's skin and firmly held in place by the coverstock's adhesive coating.

In another particularly preferred embodiment of

present invention, reservoir 16 carries a safe and effective amount of buprenorphine mixed with a skin permeation enhancing agent comprised of (a) a polar solvent material selected from the group consisting of C_3-C_4 diols, C_3-C_6 triols, and mixtures thereof; and (b), a polar lipid material selected from the group consisting of fatty alcohols, fatty acids, fatty alcohol esters, fatty acid esters, and mixtures thereof, wherein the polar solvent material and the polar lipid material are present in a weight ratio of solvent material/lipid material of from about 60:40 to about 99:1. Preferably, the polar solvent material is propylene glycol, and the polar lipid material is an ester of a C_8-C_{12} fatty alcohol or fatty acid such as methyl laurate or methyl caprylate, with the ratio of polar solvent material to polar lipid material being from about 90:10 to about 99:1. As used above, the phrase "safe and effective amount" is intended to mean the quantity of a component that is sufficient to yield a desired therapeutic response without undue adverse side effects such as toxicity, irritation, or allergic response commensurate with a reasonable benefit/risk ratio. The safe and effective amount will obviously vary depending on such factors as the particular condition or malady needing treatment, the patient's physical condition, the treatment's duration, the nature of concurrent therapy if any, and the specific formulation being used.

In the particularly preferred embodiment of the present invention, drug reservoir 16 is made from a spunbonded (nonwoven) polyester such as style number 2011 available from Reemay, Inc., P.O. Box 511, Old Hickory, TN., USA having a basis weight of 23 g/m^2 and an average thickness of 6.5 mils (0.17 mm). Other materials suitable for making drug reservoir 16 include, but are not limited to, woven and non-woven fabrics, tissues, scrims, foams, porous membranes, fibrous batting (gauze, cotton, etc.), apertured three-dimensionally expanded formed films such as those disclosed in commonly-assigned U.S. Patent Nos. 3,929,135 and 4,342,314, which are incorporated herein by reference; and other porous materials capable of holding a liquid or gel formulation in intimate contact with skin. Reservoir 16 can also take the form of a homogeneous or heterogeneous suspension of the drug and skin permeation enhancing solvents in adhesives, adhesive and non-adhesive gels, or other polymeric matrices such as natural or synthetic rubbers, thermoplastic and thermosetting polymers, hydrophilic gels, and water soluble polymers. The drug can also be mixed with a thickening or gelling agent such as hydroxypropyl cellulose to help hold the formation in place when device 10 is opened. Other suitable gelling agents include particulate and polymeric thickeners such as guar gum, methylcellulose, methylhydroxypropyl cellulose, polypropyl cellulose, starches, carboxypolymethylene, ethylene maleic anyhdride, polyacrylamide, and poly(methylvinylether-maleic anhydride). The drug is dispersed throughout matrix or reservoir 16 at a concentration preferably in excess of saturation, the amount of excess being a function of an intended useful life of the system.

It is contemplated that any drug which may be transdermally applied to a patient is suitable for use as the drug to be applied via drug reservoir 16. It will also be appreciated that the drug will not only be in the form of the pure chemical compound, but also in admixture with other drugs and/or other ingredients that are compatible with the desired objective. Thus, simple pharmacologically acceptable derivatives of the drug such as ethers, esters, amides, acetals, salts and the like may be used.

The scope of the present invention contemplates the use of a membrane (not shown) stretched across the upper surface of reservoir 16. For example, if the drug dispersed with reservoir 16 readily permeates skin, i.e., the drug inherently has a high skin flux, then a rate-controlling membrane such as those well-known in the art can be attached to the upper surface of reservoir 16. Alternatively, if the drug has a low skin flux, then a nonrate-controlling membrane can be attached to the upper surface of reservoir 16 for the purpose of holding the drug formulation in place and also to minimize the amount of the drug that is lost from reservoir 16 when upper subassembly 14 is peeled away from lower subassembly 12.

Still referring to Figures 1, 2, 3, and 4, reservoir 16 is sandwiched between upper solvent barrier film 18 and lower solvent barrier film 20. The term "solvent barrier film" is intended to mean a material that does not absorb the drug and/or skin permeation enhancing agent found in reservoir 16 to a substantial degree, an example of which includes polyester such as polyethylene terephthalate (PET). In addition, sheet barrier films 18 and 20 are preferably made from a non-stick material which acts as a release liner that minimizes the amount of the drug formulation contained in reservoir 16 that will adhere to upper solvent barrier film 18 when upper subassembly 14 is peeled away from lower subassembly 12 and discarded as will be more fully explained later. Upper solvent barrier film 18 and lower solvent barrier film 20 may be composed of the same or different material(s). Preferably, upper solvent barrier film 18 is modified, e.g., fluorinated, to provide an inert, nonwetting surface to further reduce the amount of drug formulation loss when patch 10 is opened.

In the preferred embodiment of the present invention, upper solvent barrier film 18 and lower solvent barrier film 20 are made from a laminate comprised of a layer of fluorinated polyester as the

karaya, pectins, starch, dextrin, albumin, gelatin, casein, etc. The adhesives may be compounded with tackifiers and stabilizers as is well known in the art.

Still referring to Figures 1, 2, 3, and 4, device 10 also includes release liner 40 whose upper surface is attached to the bottom surface of top cover 24 preferably by heat-sealing the two together in their areas of overlap. As best seen in Figure 3, release liner 40 is preferably provided with aperture or window 42 through which top cover 24 extends to allow top cover 24 and bottom cover 26 of compartment 22 to be hermetically sealed to one another at seal 28. The bottom surface of release liner 40 lying outside of seal 28 is in contact with the exposed adhesive layer 34' (Figures 2 and 3) on the upper surface of coverstock 32 lying outside the perimeter of bottom cover 26. Release liner 40 can be made from a wide variety of materials such as paper, waxed paper, or preferably silicone-coated kraft paper. A second, smaller piece of release liner or tab 44 is preferably interposed between release liner 40 and exposed adhesive layer 34' at one peripheral margin of device 10. Release tab 44, which also preferably includes grasping portion 46, provides an area where the user can easily start a separation (peel) between release liner 40 and coverstock 32.

In use and with reference to Figure 3, the user inserts his or her fingers between release liner 34 associated with upper subassembly 14, and release tab 44 associated with lower subassembly 12. Then, while having a firm grasp of upper subassembly 14 in one hand and lower subassembly 12 in the other, the user gently peels the two subassemblies away from each other. In the process, hermetic seal 28 between top cover 24 and bottom cover 26 of compartment 22 is gradually broken until upper subassembly 14 is fully separated from lower subassembly 12 and reservoir 16 is exposed. Finally, the user grasps portion 46 of release tab 44 and peels tab 44 away from lower subassembly 12 as shown in Figure 3, thereby fully exposing adhesive coating 34' around the perimeter of coverstock 32. After subassemblies 12 and 14 have been separated from one another as just described, the user disposes of upper subassembly 14 in a proper manner and applies lower subassembly 12 directly to the patient's skin in an area that is preferably free of hair, wrinkles, creases, or folds. Various locations on the torso such as the flank or shoulder provide suitable sites.

Those skilled in the art will now appreciate that transdermal drug delivery device 10 of the present invention is significantly different and superior to previous devices. Specifically, the transdermal patch of the present invention includes a hermetically sealed compartment that is preferably lined with a solvent barrier film so as to substantially prevent the drug formulation contained within the device from being absorbed by the device's other components or dissolving the device's other components, thereby significantly extending the storage stability and efficacy of the device. In addition, the hermetically sealed compartment and environment barrier films used in the present invention substantially protect the device's drug formulation from the adverse effects of common environmental factors such as moisture, oxygen, and light during storage, thereby also significantly extending the storage stability and efficacy of the device.

Figures 5, 6, 7, and 8 illustrate various views of another particularly preferred transdermal drug delivery device of the present invention generally indicated as 60 that includes lower subassembly generally indicated as 62, and upper subassembly generally indicated as 64. Lower subassembly 62 includes coverstock 66 which is preferably made from PVC foam or any of the other suitable materials from which previously-described coverstock 32 of patch 10 can be made. The upper surface of coverstock 66 is coated with adhesive layer 68 which similarly can be any one of the dermatologically-acceptable, pressure-sensitive adhesives as previously described in association with patch 10.

Lower subassembly 62 of patch 60 also includes lower solvent/environment barrier film 70 whose lower surface is in intimate contact with adhesive layer 68 of coverstock 66, thereby providing a strong bond therebetween. The term "solvent/environment barrier film" is intended to mean a material that does not absorb the drug and/or skin permeation enhancer found in reservoir 72 to a substantial degree and which is substantially impermeable to environmental factors such as moisture and oxygen. Drug reservoir 72, which contains the devices drug formulation and can be made from the same material as reservoir 16 of patch 10 such as a PET non-woven, is attached to the upper surface of lower barrier film 70 by, for example, heat-sealing the two together. As with previously-described transdermal device 10, the scope of the present invention contemplates the use of a rate-controlling or nonrate-controlling membrane (not shown) stretched across the upper surface of reservoir 72.

Upper subassembly 64 includes release liner 74, which is preferably made from silicone-coated kraft paper, that is provided with aperture or window 76. The bottom surface of release liner 74 is in contact with portion 68' of adhesive 68 that lies on the upper surface of coverstock 66 outside the perimeter of lower solvent/environment barrier film 70. A second small piece of release liner or tab 78 is preferably interposed between release liner 74

assembly 64 in one hand and lower subassembly 62 in the other, the user gently peels the two subassemblies away from each other. In the process, hermetic seal 84 between lower barrier film 70 and upper barrier film 80 is gradually broken until upper subassembly 64 is fully separated from lower subassembly 62 and reservoir 72 is exposed. Finally, the user grasps portion 79 of release tab 44 and peels tab 44 away from lower subassembly 62 as shown in Figure 7, thereby fully exposing adhesive coating 68 around the perimeter of coverstock 66. After subassemblies 62 and 64 have been fully separated from one another as just described, the user disposes of upper subassembly 64 in a proper manner and applies lower subassembly 62 directly to the patient's skin.

In some instances, it may be advantageous to maintain device 10 or 60 of the present invention in a sterile condition and/or to further protect device 10 or device 60 from common environmental factors by placing each device or a small group of devices within an outer protective overpouch or overwrap. Such overpouches or overwraps, which are commonly used in the medical industry to protect other types of bandages, gauzes, and instruments, can be made from a wide variety of materials and typically include at least one layer of a metal foil having graphics, instructions, etc. printed thereon.

EXAMPLE 1

The following procedure describes an example of how to assemble transdermal drug delivery device 10 of the present invention, each device having an upper subassembly 14, a lower subassembly 12 that contains the drug formulation, and a hermetic seal joining the two subassemblies together.

In making lower subassembly 12, compartment bottom cover 26 was first made by using a paper cutter to cut a 6" x 4" (15.2 cm x 10.2 cm) sheet from a rollstock of skintone heat-sealable polyester film laminate, product number 1006 obtained from 3M Health Care Specialties, 6850 S. Harlem Ave., Bedford Park, Illinois USA. This laminate sheet was placed with its machine direction aligned with the long dimension of blades of an oval rule die and covered first with a piece of cardboard and then a piece of 1/4" (0.64 cm) Lexan®. The die was then placed in a Carver press and subjected to a pressure of 5000 psig which cut compartment bottom cover 26 from the sheet. Cover 26 was generally oval in shape, 5" (12.7 cm) long by 2 1/4" (5.7 cm) wide and having rounded ends, each with a 1 1/8" (2.9 cm) radius.

Lower barrier film 20 of lower subassembly 12 was made by placing a 6" x 4" (15.2 cm x 10.2 cm) sheet of transparent Scotchpak® heat-sealable polyester film laminate, product number 1220 also obtained from 3M Health Care Specialties, on the blades of a rule die, which was then covered with a piece of cardboard and a sheet of 1/4" (0.64 cm) Lexan®. The die was placed in a Carver press and subjected to a pressure of 5000 psig which cut lower barrier film 20 from the sheet. Lower barrier film 20 was generally oval in shape, 4" (10.2 cm) long by 1 1/4" (3.2 cm) wide and having rounded ends, each with a 5/8" (1.6 cm) radius.

Reservoir 16 was made by placing a 6" x 4" (15.2 cm x 10.2 cm) sheet of Reemay spunbonded polyester (style number 2011, basis weight 23 g/m^2, average thickness 6.5 mils (0.17 mm) obtained from Reemay Inc., P.O. Box 511, Old Hickory, TN, USA on the blades of a rule die which was then covered with a sheet of cardboard and Lexan®. The die was placed in a Carver press and subjected to a pressure of 5000 psig which cut reservoir 16 from the polyester sheet. Reservoir 16 was generally oval in shape, 4 1/4" (10.8 cm) long by 1 1/2" (3.8 cm) wide and having rounded ends, each with a 3/4" (1.9 cm) radius.

To heat seal lower barrier film 20 to the inner surface of compartment bottom cover 26, a teflon-coated heat-sealing die with an oval perimeter .56" (1.4 cm) wide seal land was attached and registered to the top platen of a Sentinel heat sealer, model number 808, obtained from Packaging Industries, Hyannis, MA, USA, which was set at 200° F (93° C), 80 psig, 4 second dwell. A piece of 70 durometer silicone rubber (1/32" thick) was placed on a puck designed to slide in and out from between the platens of the press. A cardboard template of the lower barrier film 20 was placed on the silicone rubber on the puck and aligned with the heat sealing die. Lower barrier film 20 was placed heat seal side up on the silicone rubber using the template for alignment. The barrier film template was removed and a template of compartment bottom cover 26 was placed on the puck and aligned with the heat sealing die. Compartment bottom cover 26 was then placed heat seal side down over lower barrier film 20 using the template for alignment, which was then removed from the puck. The puck was placed in the press which was energized and sealed lower barrier film 20 to compartment bottom cover 26.

The outer peripheral edge of reservoir 16 was heat-sealed to compartment bottom cover 26, which had been lined with lower barrier film 20 as just described. In attaching reservoir 16 to cover 26, a teflon-coated, heat-sealing die with an oval perimeter 1/8" (0.32 cm) wide seal land was attached and registered to the top platen of the

The gel was then transferred to a brown glass jar and blanketed with dry nitrogen before sealing with a solvent resistant screw cap.

With the use of a micro-pipette, 700 mg of the gel was applied to reservoir 16 area of lower subassembly 14. This step was carried out inside a glove box maintained at less than 10% relative humidity.

The final assembly of patch 10 consisted of heat-sealing lower subassembly 12 to upper subassembly 14 by forming hermetic seal 28 therebetween. A teflon-coated heat sealing die with an oval sealing land being 4.5" (11.43 cm) long, 1.75" (4.45 cm) wide and having a 7/8" (2.22 cm) radius on each rounded end, was attached and registered to the top platen of the press. The land width of this die was .040" (.1 cm). The press was set at 286° F (140° C)m, 65 psig and 0.7 second dwell. A cardboard template of lower subassembly 12 was placed on the puck and aligned with the heat sealing die. Lower subassembly 12 was placed heat seal side up on the puck using the template for alignment. The template was then removed. Upper subassembly 14 was then placed on the puck, heat seal side down, over lower subassembly 12 and aligned with the heat sealing die. The puck was then placed in the press and the press was activated to hermetically seal the subassemblies together.

A 7" x 4.5" (17.78 cm x 11.4 cm) sheet of PVC microfoam tape (product number 9772-L) obtained from 3M Health Care Specialties, was cut on a paper cutter. The release paper was removed and the coverstock was placed, adhesive side down, over compartment bottom cover 26 of the sealed subassemblies. This sheet was then placed on the blades of a rule die and aligned. It was covered with a piece of cardboard and a piece of 1/4" (.635 cm) Lexan®. The die was then placed in a Carver Press and the pressure was increased to 5000 psig which cut complete patch 10 from the sheet. Patch 10 was approximately oval in shape with the dimensions being 6.75" (17.2 cm) long by 4.0" (10.2 cm) wide and having rounded ends, each with a 2" (5.1 cm) radius.

A pull tab was die cut from 3 lb. release liner, poly-coated one side, silicone-coated one side (product number 1361) obtained from 3M Health Care Specialties. This was applied to the patch by adhering the silicone-coated side to the adhesive on the coverstock on one of the rounded ends.

EXAMPLE II

The following procedure describes an example of how to assemble transdermal patch 60 of the present invention, each patch consisting of lower subassembly 62 which contained the drug formulation, upper subassembly 64, and hermetic seal 84 joining the two subassemblies together.

In making lower barrier film 70 of lower subassembly 62, a sheet of heat-sealable, polyester film laminate (product number PT-15-100) obtained from the Presto Products Company of Appleton, WI, USA, was placed over the blades of a rule die and covered with a piece of cardboard and then a piece of 1/4" (.635 cm) Lexan®. The die was placed in a Carver press and subjected to a pressure of 5000 psig which cut lower barrier film 70 from the sheet. Lower barrier film 70 was circular in shape and approximately 2 1/4" (5.72 cm) in diameter.

In making reservoir 72, a sheet of Reemay spunbonded polyester, (style number 2011, basis wt. 23 g/m², average thickness 6.5 mils) obtained from Reemay, Inc. was placed on the blades of a rule die and covered with a piece of cardboard and then a piece of 1/4" (.635 cm) Lexan®. The die was placed in a Carver press and subjected to a pressure of 5000 psig which cut reservoir 72 from the sheet. Reservoir 72 was circular in shape and approximately 1 7/16" (3.65 cm) in diameter).

To heat seal reservoir 72 to lower barrier film 70, a teflon-coated heat sealing die with a perimeter .108" (.273 cm) wide seal land was attached and registered to the top platen of the press. The press was set at 325° F (163° C), 50 psig and 0.4 second dwell. A cardboard template of reservoir 72 was placed on the puck and aligned with the heat sealing die by using the template. The template was then removed and a template of lower barrier film 70 was placed on the puck and aligned with the heat sealing die. A lower barrier film 70 was placed heat seal side down over reservoir 72 using the template for alignment. The template was removed from the puck and lower barrier film 70 was then covered with a piece of .004" (0.10 cm) thick CHR Temp-R-Glass obtained from Cincinnati Gasket of Cincinnati, Ohio, USA. This was used to facilitate the release of components from the die. The puck was placed in the press and the press activated to seal reservoirs 72 to the compartment tops.

To begin making upper subassembly 64, a sheet of heat sealable, polyester film laminate (product number PT-20-100) also obtained from the Presto Products Company was placed over the blades of a rule die and covered with a piece of cardboard and then 1/4" (.635 cm) Lexan®. The die was placed in a Carver press and subjected to a pressure of 5000 psig which cut upper barrier film 80 from the sheet. Upper barrier film 80 was circular in shape and approximately 2 9/16" (6.51 cm) in diameter.

by peeling said release liner from said coverstock opens said compartment, thereby exposing said reservoir member and the medicament contained there.

2. A storage-stable device for the transdermal delivery of an active pharmaceutical, said device being characterized by: a drug reservoir member containing a quantity of a transdermal medicament which includes an effective amount of said pharmaceutical, said reservoir member having an upper surface and a lower surface; a lower solvent/environment barrier film in contact with said lower surface of said reservoir member; an upper solvent/environment barrier film in contact with said upper surface of said reservoir member, said lower and said upper solvent/environment barrier films being sealed together near their peripheral edges to define a hermetically sealed compartment therebetween; an outermost coverstock attached to said lower solvent/environment barrier film, said coverstock having an adhesive coating thereon, said hermetically sealed lower and upper solvent/environment barrier films preventing said medicament from coming into contact with said adhesive coating on said coverstock; and a release liner attached to said upper solvent/environment barrier film and adhesively adhered to the periphery of said coverstock, whereby peeling said release liner from said coverstock opens said compartment thereby exposing said reservoir member and the medicament contained therein.

3. The transdermal device according to either of Claims 1 and 2 wherein a release tab is interposed between said adhesive-coated coverstock and said release liner at an outer marginal portion of said device.

4. The transdermal device according to either of Claims 1 and 2, wherein a rate-controlling or nonrate-controlling membrane may optionally be disposed between said reservoir member and said upper barrier film.

5. The transdermal device according to either of Claims 1 and 2 wherein said barrier films are made from a laminate comprised of an outer heat-sealable layer and an inner reservoir-member-contacting layer.

6. The transdermal device according to Claim 5 wherein said inner reservoir-member-contacting layer is made from a material selected from the group consisting of polyethylene terephthalate, fluorinated polyethylene terephthalate, a rubber modified acrylonitrile copolymer, nylon, EVOH, styrene acrylonitrile copolymer, polyvinylidine chloride copolymer, and polychlorotrifluoroethylene copolymer.

7. The transdermal device according to Claim 1 wherein said top cover and said bottom cover of said compartment are made from a laminate comprised of an outer heat-sealable layer, at least one intermediate environment barrier layer, and an inner heat-sealable layer.

8. The transdermal device according to Claim 7 wherein said environment barrier layer is selected from the group consisting of polyethylene terephthalate, metallized polyethylene terephthalate, metal foils, a polyvinylidine chloride copolymer, a rubber modified acrylonitrile copolymer, nylon, EVOH, and polychlorotrifluoroethylene copolymer.

9. The transdermal device according to either of Claims 1 and 2 wherein said medicament includes a skin permeation enhancing agent, said skin permeation enhancing agent being selected from the group consisting of polar solvent materials, polar lipid materials, and mixtures thereof.

10. The transdermal device according to Claim 9 wherein said polar solvent materials are selected from the group consisting of C_3-C_4 diols, C_3-C_6 triols, and mixtures thereof; and wherein said polar lipid materials are selected from the group consisting of fatty alcohols, fatty acids, fatty alcohol esters, fatty acid esters, and mixtures thereof.

11. The transdermal device according to Claim 9 wherein said polar solvent material is propylene glycol, and wherein said polar lipid material is methyl laurate or methyl caprylate.

Fig. 1

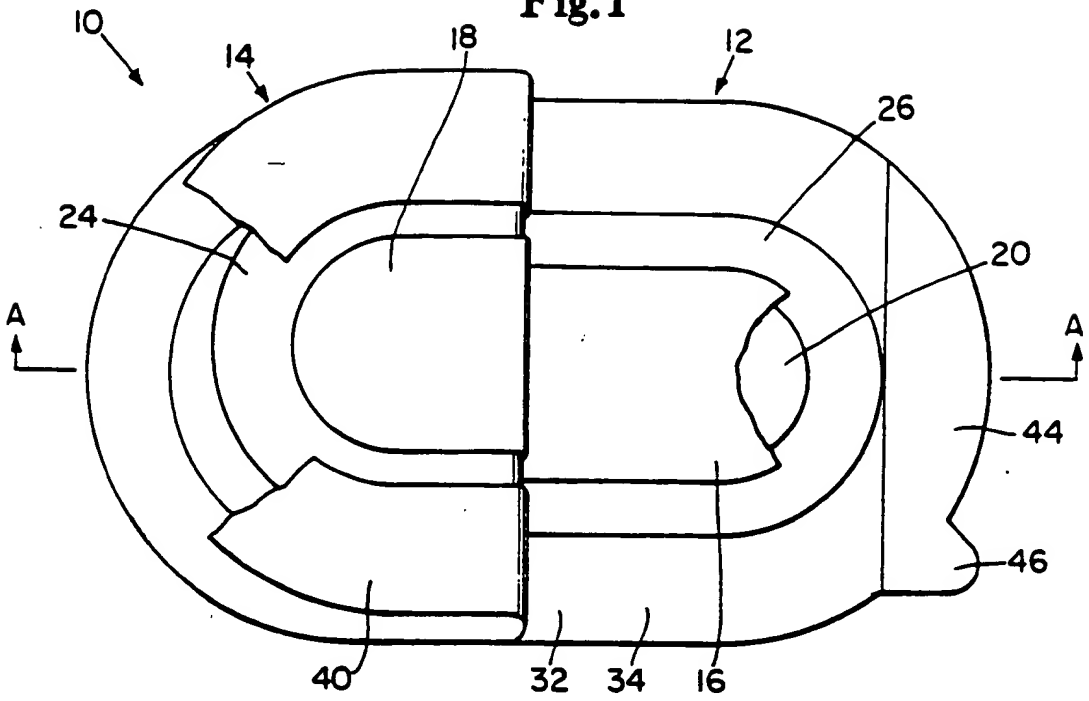


Fig. 2

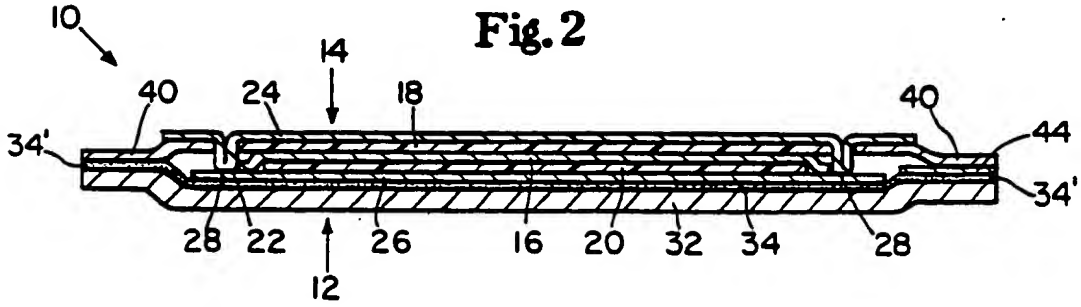
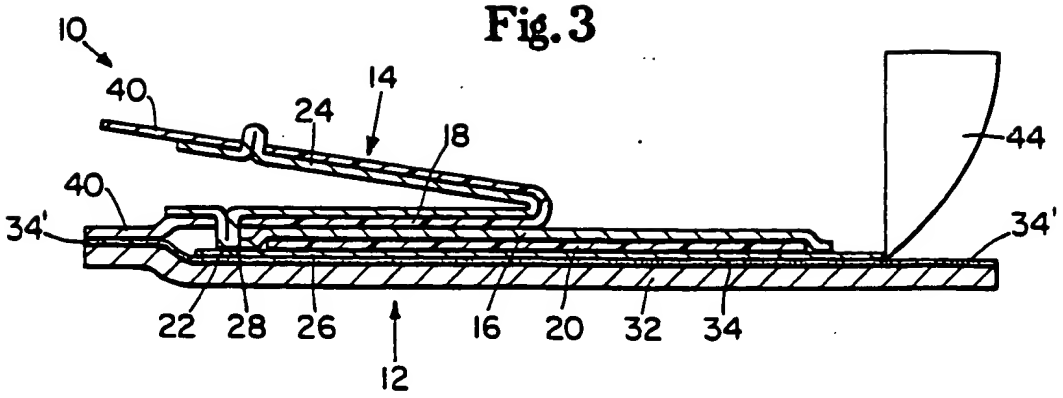


Fig. 3



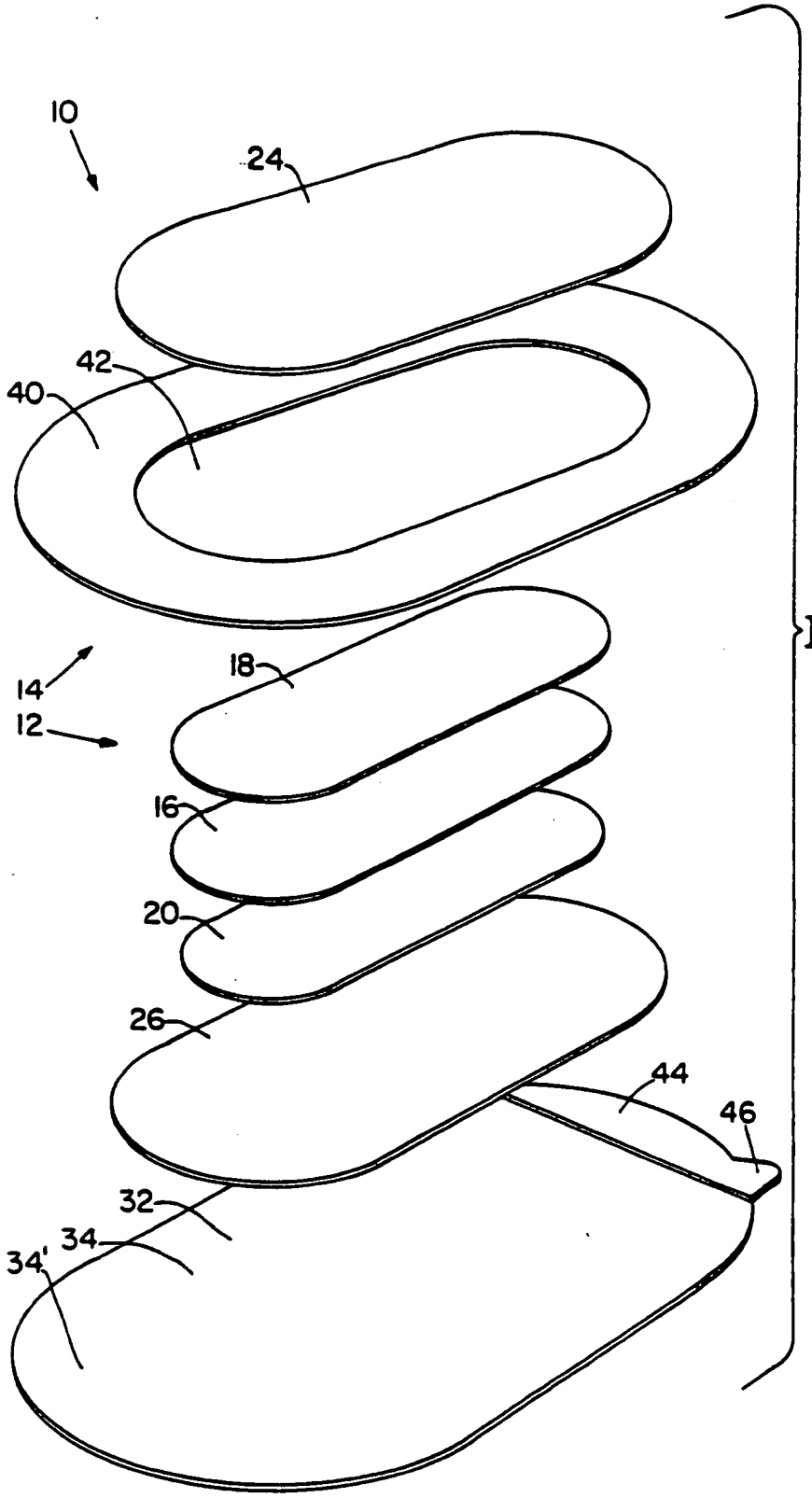


Fig. 4

Fig.5

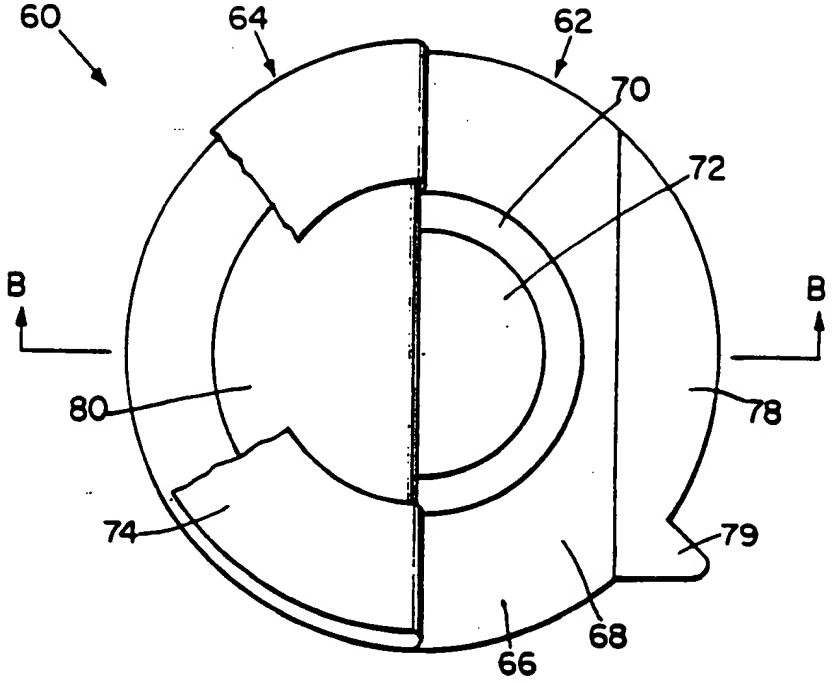


Fig.6

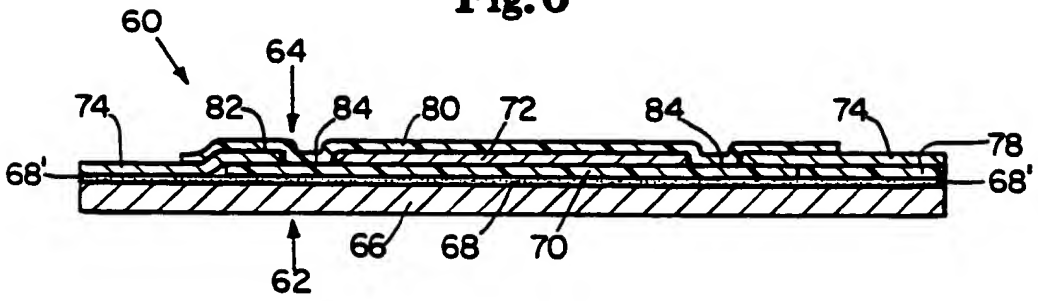
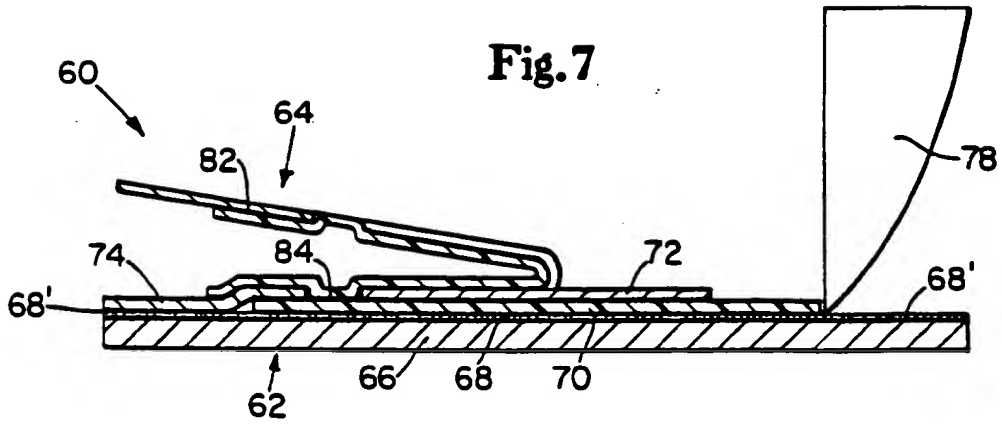


Fig.7



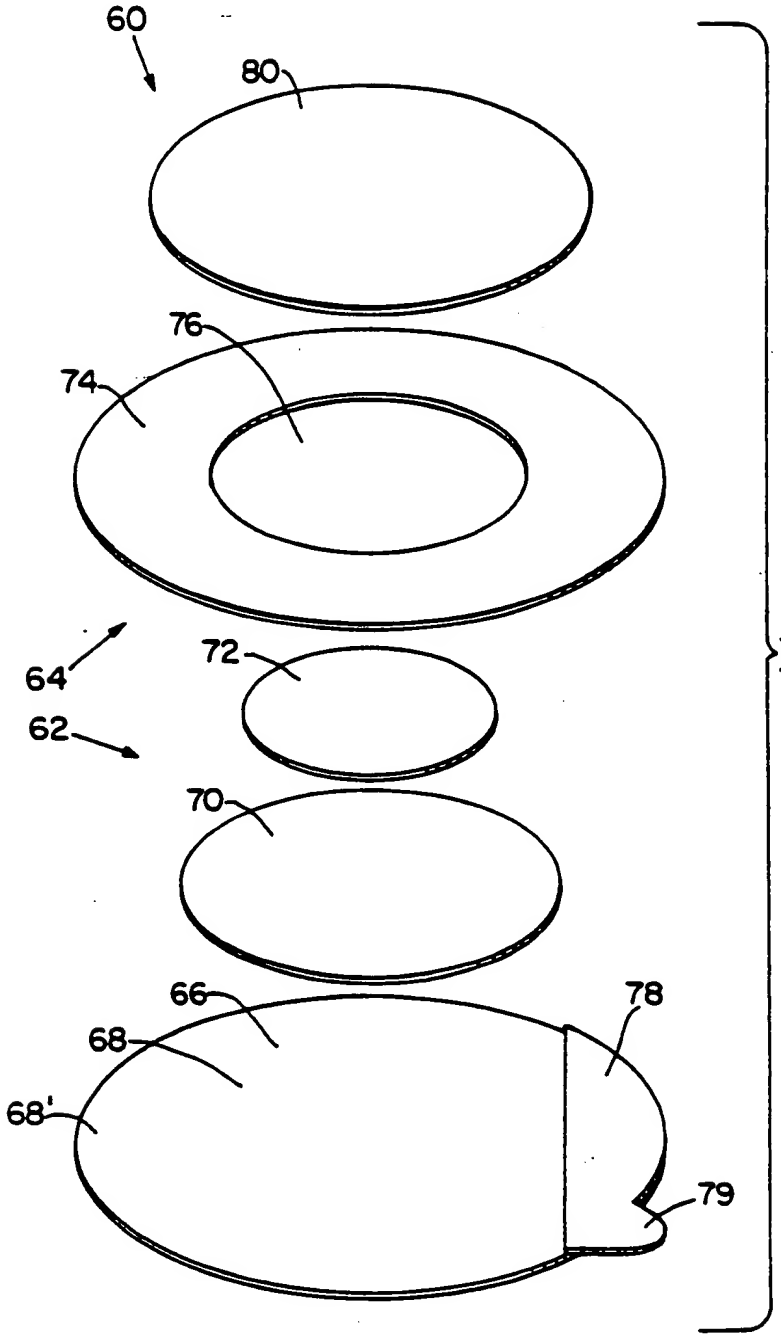


Fig. 8